```
=> fil reg; d ide
FILE 'REGISTRY' ENTERED AT 12:39:37 ON 21 NOV 2002
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   20 NOV 2002  HIGHEST RN 474043-36-2
DICTIONARY FILE UPDATES:  20 NOV 2002  HIGHEST RN 474043-36-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf



L14  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   [redacted]  REGISTRY
CN   Synthetase, prostaglandin endoperoxide, 2 (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Arachidonate cyclooxygenase 2
CN   COX 2
CN   [redacted]
CN   Prostaglandin endoperoxide H synthase-2
CN   Prostaglandin endoperoxide synthase-2
CN   Prostaglandin endoperoxide synthetase 2
CN   Prostaglandin G/H synthase-2
CN   Prostaglandin H synthase-2
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   BIOSIS, CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            1632 REFERENCES IN FILE CA (1962 TO DATE)
               2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1686 REFERENCES IN FILE CAPLUS (1962 TO DATE)


=> d ide

L15  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   53847-30-6  REGISTRY
CN   5,8,11,14-Eicosatetraenoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester,
     (5Z,8Z,11Z,14Z)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   5,8,11,14-Eicosatetraenoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester,
     (all-Z)-
OTHER NAMES:
CN   2-Arachidonylglycerol
FS   STEREOSEARCH
DR   75656-17-6
MF   C23 H38 O4
```
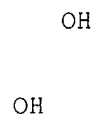

LC STN Files: AGRICOLA, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CHEMCATS, CSCHEM, MEDLINE, TOXCENTER, USPAT2, USPATFULL

Double bond geometry as shown.

PAGE 1-A

PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

163 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
164 REFERENCES IN FILE CAPLUS (1962 TO DATE)

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=> fil capl; d que l22; d que l25;d que l26
FILE 'CAPLUS' ENTERED AT 13:59:20 ON 21 NOV 2002
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FILE COVERS 1907 - 21 Nov 2002  VOL 137 ISS 21
FILE LAST UPDATED: 20 Nov 2002  (20021120/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

L14           1 SEA FILE=REGISTRY ABB=ON  CYCLOOXYGENASE 2/CN
L16        1687 SEA FILE=CAPLUS ABB=ON  L14
L17        4237 SEA FILE=CAPLUS ABB=ON  (CYCLOOXYGENASE OR CYCLO OXYGENASE OR
                COX OR PROSTAGLANDIN(2W)(SYNTHASE OR SYNTHETASE))(W)(2 OR
                II)/OBI
L20       55096 SEA FILE=CAPLUS ABB=ON  PROSTAGLANDIN#/OBI
L21           6 SEA FILE=CAPLUS ABB=ON  L20(L)GLYCEROL(L)ESTER?
L22           2 SEA FILE=CAPLUS ABB=ON  (L16 OR L17) AND L21


L15           1 SEA FILE=REGISTRY ABB=ON  53847-30-6
L18         165 SEA FILE=CAPLUS ABB=ON  L15
L19         124 SEA FILE=CAPLUS ABB=ON  2(W)(ARACHIDONYLGLYCEROL OR ARACHIDONYL
                GLYCEROL)
L20       55096 SEA FILE=CAPLUS ABB=ON  PROSTAGLANDIN#/OBI
L21           6 SEA FILE=CAPLUS ABB=ON  L20(L)GLYCEROL(L)ESTER?
L24      133486 SEA FILE=CAPLUS ABB=ON  MASS SPECTR?/OBI
L25           5 SEA FILE=CAPLUS ABB=ON  (L18 OR L19 OR L21) AND L24


L15           1 SEA FILE=REGISTRY ABB=ON  53847-30-6
L18         165 SEA FILE=CAPLUS ABB=ON  L15
L19         124 SEA FILE=CAPLUS ABB=ON  2(W)(ARACHIDONYLGLYCEROL OR ARACHIDONYL
                GLYCEROL)
L20       55096 SEA FILE=CAPLUS ABB=ON  PROSTAGLANDIN#/OBI
L21           6 SEA FILE=CAPLUS ABB=ON  L20(L)GLYCEROL(L)ESTER?
L24      133486 SEA FILE=CAPLUS ABB=ON  MASS SPECTR?/OBI
L26           4 SEA FILE=CAPLUS ABB=ON  (L18 OR L19 OR L21)(L)ANST/RL AND L24
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Role - ANST = analytical study

=> s l22 or l25 or l26

L99 6 L22 OR L25 OR L26

=> fil medl; d que l35; d que l39

FILE 'MEDLINE' ENTERED AT 13:59:22 ON 21 NOV 2002

FILE LAST UPDATED: 20 NOV 2002 (20021120/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

If you received SDI results from MEDLINE on October 8, 2002, these may have included old POPLINE data and in some cases duplicate abstracts. For further information on this situation, please visit NLM at: http://www.nlm.nih.gov/pubs/techbull/so02/so02_popline.html

To correct this problem, CAS will remove the POPLINE records from the MEDLINE file and process the SDI run dated October 8, 2002 again.

Customers who received SDI results via email or hard copy prints on October 8, 2002 will not be charged for this SDI run. If you received your update online and displayed answers, you may request a credit by contacting the CAS Help Desk at 1-800-848-6533 in North America or 614-447-3698 worldwide, or via email to help@cas.org

This file contains CAS Registry Numbers for easy and accurate substance identification.

L29	5691	SEA FILE=MEDLINE ABB=ON	(CYCLOOXYGENASE OR CYCLO OXYGENASE OR COX OR PROSTAGLANDIN(2W)(SYNTHASE OR SYNTHETASE))(W)(2 OR II)
L30	69325	SEA FILE=MEDLINE ABB=ON	PROSTAGLANDINS+NT/CT
L31	294	SEA FILE=MEDLINE ABB=ON	GLYCEROL(2A)ESTER?
L32	8486	SEA FILE=MEDLINE ABB=ON	ESTERS/CT
L33	3	SEA FILE=MEDLINE ABB=ON	PROSTAGLANDIN?(3A)GLYCEROL(3A)ESTER?
L35	**5**	**SEA FILE=MEDLINE ABB=ON**	**L29 AND (L31 OR (L32 AND L30) OR L33)**

L29	5691	SEA FILE=MEDLINE ABB=ON	(CYCLOOXYGENASE OR CYCLO OXYGENASE OR COX OR PROSTAGLANDIN(2W)(SYNTHASE OR SYNTHETASE))(W)(2 OR II)
L34	155	SEA FILE=MEDLINE ABB=ON	2(W)(ARACHIDONYLGLYCEROL OR ARACHIDONYL GLYCEROL)
L37	7686	SEA FILE=MEDLINE ABB=ON	PROSTAGLANDIN-ENDOPEROXIDE SYNTHASE/CT
L38	533	SEA FILE=MEDLINE ABB=ON	L37(L)(AN OR CH)/CT
L39	**2**	**SEA FILE=MEDLINE ABB=ON**	**L29 AND L38 AND L34**

- Subheadings
AN = analysis
CH = chemistry

=> s l35 or l39

L100 5 L35 OR L39

=> fil embase; d que l43; d que l54; d que l57

FILE 'EMBASE' ENTERED AT 13:59:24 ON 21 NOV 2002

FILE COVERS 1974 TO 14 Nov 2002 (20021114/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L43 1 SEA FILE=EMBASE ABB=ON PROSTAGLANDIN GLYCEROL ESTER DERIVATIVE /CT

L40 3544 SEA FILE=EMBASE ABB=ON CYCLOOXYGENASE 2/CT
L44 764 SEA FILE=EMBASE ABB=ON PROSTAGLANDIN METABOLISM/CT
L45 168 SEA FILE=EMBASE ABB=ON 2 ARACHIDONOYLGLYCEROL/CT
L46 13 SEA FILE=EMBASE ABB=ON 2 ARACHIDONYL GLYCEROL/CT OR 2 ARACHIDONYLGLYCEROL/CT
L54 1 SEA FILE=EMBASE ABB=ON L40 AND L44 AND (L45 OR L46)

L40 3544 SEA FILE=EMBASE ABB=ON CYCLOOXYGENASE 2/CT
L41 1015 SEA FILE=EMBASE ABB=ON PROSTAGLANDIN F1 ALPHA/CT
L42 22710 SEA FILE=EMBASE ABB=ON PROSTAGLANDIN/CT
L56 7 SEA FILE=EMBASE ABB=ON (L41 OR L42) AND GLYCEROL AND ESTER?
L57 0 SEA FILE=EMBASE ABB=ON L56 AND L40

=> s l43 or l54

L101 1 L43 OR L54

=> fil wpids; d que l63; d que l67

FILE 'WPIDS' ENTERED AT 13:59:25 ON 21 NOV 2002
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FILE LAST UPDATED: 20 NOV 2002 <20021120/UP>
MOST RECENT DERWENT UPDATE: 200275 <200275/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>

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>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

L59 689 SEA FILE=WPIDS ABB=ON (CYCLOOXYGENASE OR CYCLO OXYGENASE OR COX OR PROSTAGLANDIN(2W)(SYNTHASE OR SYNTHETASE))(W)(2 OR II)
L60 5 SEA FILE=WPIDS ABB=ON PROSTAGLANDIN?(3A)GLYCER?(3A)ESTER?
L61 8 SEA FILE=WPIDS ABB=ON ARACHIDONYL GLYCEROL OR ARACHIDONYLGLYCEROL
L62 4 SEA FILE=WPIDS ABB=ON ARACHIDONOYLGLYCEROL OR ARACHIDONOYL GLYCEROL

L63 2 SEA FILE=WPIDS ABB=ON L59 AND (L60 OR L61 OR L62)

L59 689 SEA FILE=WPIDS ABB=ON (CYCLOOXYGENASE OR CYCLO OXYGENASE OR COX OR PROSTAGLANDIN(2W)(SYNTHASE OR SYNTHETASE))(W)(2 OR II)
L64 3885 SEA FILE=WPIDS ABB=ON METABOLITE#
L65 227362 SEA FILE=WPIDS ABB=ON ACTIVIT?
L66 81 SEA FILE=WPIDS ABB=ON L59(5A)L65
L67 4 SEA FILE=WPIDS ABB=ON L66 (P)L64

=> s l63 or l67

L102 4 L63 OR L67

=> fil biotechno; d que l71

FILE 'BIOTECHNO' ENTERED AT 13:59:28 ON 21 NOV 2002
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FILE LAST UPDATED: 19 NOV 2002 <20021119/UP>
FILE COVERS 1980 TO DATE.

>>> SIMULTANEOUS LEFT AND RIGHT TRUNCATION AVAILABLE IN /CT AND BASIC INDEX <<<

L71 1 SEA FILE=BIOTECHNO ABB=ON PROSTAGLANDIN?(3A)GLYCER?(3A)ESTER?

=> fil scisearch; d que l88

FILE 'SCISEARCH' ENTERED AT 13:59:30 ON 21 NOV 2002
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FILE COVERS 1974 TO 15 Nov 2002 (20021115/ED)

L88 3 SEA FILE=SCISEARCH ABB=ON PROSTAGLANDIN?(3A)GLYCER?(3A)ESTER?

=> fil biosis; d que l92

FILE 'BIOSIS' ENTERED AT 13:59:31 ON 21 NOV 2002
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 20 November 2002 (20021120/ED)

L92 5 SEA FILE=BIOSIS ABB=ON PROSTAGLANDIN?(3A)GLYCER?(3A)ESTER?

=> dup rem l100,l99,l92,l71,l101,l88,l102
FILE 'MEDLINE' ENTERED AT 14:00:56 ON 21 NOV 2002

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FILE 'WPIDS' ENTERED AT 14:00:56 ON 21 NOV 2002
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PROCESSING COMPLETED FOR L100
PROCESSING COMPLETED FOR L99
PROCESSING COMPLETED FOR L92
PROCESSING COMPLETED FOR L71
PROCESSING COMPLETED FOR L101
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L102
L103 15 DUP REM L100 L99 L92 L71 L101 L88 L102 (10 DUPLICATES REMOVED)
ANSWERS '1-5' FROM FILE MEDLINE
ANSWERS '6-10' FROM FILE CAPLUS
ANSWERS '11-12' FROM FILE BIOSIS
ANSWERS '13-15' FROM FILE WPIDS

=> d ibib ab hitrn 1-15

L103 ANSWER 1 OF 15 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001547033 MEDLINE
DOCUMENT NUMBER: 21463029 PubMed ID: 11447235
TITLE: Metabolism of **prostaglandin glycerol esters** and **prostaglandin** ethanolamides in vitro and in vivo.
AUTHOR: Kozak K R; Crews B C; Ray J L; Tai H H; Morrow J D; Marnett L J
CORPORATE SOURCE: Department of Biochemistry and Chemistry, Vanderbilt-Ingram Cancer Center and Center in Molecular Toxicology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: CA77839 (NCI)
DK48831 (NIDDK)
GM15431 (NIGMS)
HL46296 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Oct 5) 276 (40) 36993-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011015
Last Updated on STN: 20020122
Entered Medline: 20011204
AB **Prostaglandin glycerol esters** (PG-Gs) and

prostaglandin ethanolamides (PG-EAs) are generated by the action of **cyclooxygenase-2** on the endocannabinoids 2-arachidonylglycerol (2-AG) and arachidonylethanolamide, respectively. These novel eicosanoids may have unique pharmacological properties and/or serve as latent sources of prostaglandins at sites remote from their tissue of origin. Therefore, we investigated the metabolism of PG-Gs and PG-EAs in vitro and in vivo. PGE(2)-G was rapidly hydrolyzed in rat plasma to generate PGE(2) (t(1/2) = 14 s) but was only slowly metabolized in human plasma (t(1/2) > 10 min). An intermediate extent of metabolism of PGE(2)-G was observed in human whole blood (t(1/2) approximately 7 min). The parent arachidonylglycerol, 2-AG, and the more stable regioisomer, 1-AG, also were much more rapidly metabolized in rat plasma compared with human plasma. PGE(2)-EA was not significantly hydrolyzed in plasma, undergoing slow dehydration/isomerization to PGB(2)-EA. Both PGE(2)-G and PGE(2)-EA were stable in canine, bovine, and human cerebrospinal fluid. Human 15-hydroxyprostaglandin dehydrogenase, the enzyme responsible for the initial step in PG inactivation in vivo, oxidized both PGE(2)-G and PGE(2)-EA less efficiently than the free acid. The sterically hindered glyceryl prostaglandin was the poorest substrate examined in the E series. Minimal 15-hydroxyprostaglandin dehydrogenase oxidation of PGF(2 alpha)-G was observed. PGE(2)-G and PGE(2)-EA pharmacokinetics were assessed in rats. PGE(2)-G was not detected in plasma 5 min following an intravenous dose of 2 mg/kg. However, PGE(2)-EA was detectable up to 2 h following an identical dose, displaying a large apparent volume of distribution and a half-life of over 6 min. The results suggest that endocannabinoid-derived PG-like compounds may be sufficiently stable in humans to exert actions systemically. Furthermore, these results suggest that the rat is not an adequate model for investigating the biological activities of 2-arachidonylglycerol or glyceryl prostaglandins in humans.

L103 ANSWER 2 OF 15 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2001441659 MEDLINE
DOCUMENT NUMBER: 21380188 PubMed ID: 11402053
TITLE: Amino acid determinants in **cyclooxygenase-2** oxygenation of the endocannabinoid **2-arachidonylglycerol**.
AUTHOR: Kozak K R; Prusakiewicz J J; Rowlinson S W; Schneider C; Marnett L J
CORPORATE SOURCE: Departments of Biochemistry and Chemistry, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: CA68484 (NCI)
CA89450 (NCI)
ES00267 (NIEHS)
GM07347 (NIGMS)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Aug 10) 276 (32) 30072-7.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010910
Entered Medline: 20010906

AB The endocannabinoid, **2-arachidonylglycerol** (2-AG), is an endogenous ligand for the central (CB1) and peripheral (CB2) cannabinoid receptors and has been shown to be efficiently and selectively oxygenated by cyclooxygenase (**COX**)-**2**. We have investigated 2-AG/**COX-2** interactions through site-directed mutagenesis. An evaluation of more than 20 site-directed mutants of murine **COX-2** has allowed for the

development of a model of 2-AG binding within the **COX-2** active site. Most strikingly, these studies have identified Arg-513 as a critical determinant in the ability of **COX-2** to efficiently generate **prostaglandin** H(2) **glycerol ester**, explaining, in part, the observed isoform selectivity for this substrate. Mutational analysis of Leu-531, an amino acid located directly across from Arg-513 in the **COX-2** active site, suggests that 2-AG is shifted in the active site away from this hydrophobic residue and toward Arg-513 relative to arachidonic acid. Despite this difference, aspirin-treated **COX-2** oxygenates 2-AG to afford 15-hydroxyeicosatetraenoic acid **glycerol ester** in a reaction analogous to the C-15 oxygenation of arachidonic acid observed with acetylated **COX-2**. Finally, the differences in substrate binding do not alter the stereospecificity of the cyclooxygenase reaction; 2-AG-derived and arachidonic acid-derived products share identical stereochemistry.

L103 ANSWER 3 OF 15 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2001038259 MEDLINE
DOCUMENT NUMBER: 20517939 PubMed ID: 10931854
TITLE: Oxygenation of the endocannabinoid, **2-arachidonylglycerol**, to glyceryl prostaglandins by **cyclooxygenase-2**.
AUTHOR: Kozak K R; Rowlinson S W; Marnett L J
CORPORATE SOURCE: Departments of Biochemistry and Chemistry, Vanderbilt-Ingram Cancer Center and Center in Molecular Toxicology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232, USA.
CONTRACT NUMBER: CA47479 (NCI)
CA68484 (NCI)
ES00267 (NIEHS)
+
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Oct 27) 275 (43) 33744-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20001124

AB Cyclooxygenases (COX) play an important role in lipid signaling by oxygenating arachidonic acid to endoperoxide precursors of prostaglandins and thromboxane. Two cyclooxygenases exist which differ in tissue distribution and regulation but otherwise carry out identical chemical functions. The neutral arachidonate derivative, **2-arachidonylglycerol** (2-AG), is one of two described endocannabinoids and appears to be a ligand for both the central (CB1) and peripheral (CB2) cannabinoid receptors. Here we report that 2-AG is a substrate for **COX-2** and that it is metabolized as effectively as arachidonic acid. **COX-2**-mediated 2-AG oxygenation provides the novel lipid, **prostaglandin** H(2) **glycerol ester** (PGH(2)-G), in vitro and in cultured macrophages. PGH(2)-G produced by macrophages is a substrate for cellular PGD synthase, affording PGD(2)-G. Pharmacological studies reveal that macrophage production of PGD(2)-G from endogenous sources of 2-AG is calcium-dependent and mediated by diacylglycerol lipase and **COX-2**. These results identify a distinct function for **COX-2** in endocannabinoid metabolism and in the generation of a new family of prostaglandins derived from diacylglycerol and 2-AG.

L103 ANSWER 4 OF 15 MEDLINE
ACCESSION NUMBER: 2001372414 MEDLINE
DOCUMENT NUMBER: 21322112 PubMed ID: 11429387
TITLE: Generation of 8-epi-prostaglandin F(2alpha) in isolated rat kidney glomeruli by a radical-independent mechanism.
AUTHOR: Klein T; Neuhaus K; Reutter F; Nusing R M
CORPORATE SOURCE: Department of Pediatrics, Philipps-University of Marburg, D-35033 Marburg, Germany.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (2001 Jul) 133 (5) 643-50. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20020420
Entered Medline: 20010809

AB Isoprostanes comprise a group of free radical-catalyzed products of arachidonic acid. However, there is recent evidence pointing towards an enzyme-dependent formation of isoprostanes. With the use of isolated rat glomeruli we addressed the mechanisms of isoprostane generation. Synthesis of prostanoids and isoprostanes, including 8-epi-PGF(2alpha), was studied under conditions favouring radical formation. Cultured glomeruli formed different prostanoids including 8-epi-PGF(2alpha). Upon LPS challenge cyclo-oxygenase (**COX**)-**2** expression was enhanced, and this was paralleled by a 2 - 9-fold increase in prostanoid formation, including isoprostanes. Addition of COX-isoform unselective inhibitors (diclofenac, indomethacin) or a selective inhibitor (NS-398) suppressed the synthesis of prostanoids, 8-epi-PGF(2alpha) and total isoprostane fraction; however, inhibition of the latter was less pronounced. Antioxidants such as butylated hydroxytoluene (BHT), nordihydroguaiaretic acid (NDGA), or dimethylurea exhibited an only minimal inhibitory effect on 8-epi-PGF(2alpha) synthesis. Moreover, ROS-generating drugs (menadione, methylviologen) or NADPH-driven radical formation were unable to cause the generation of significant amounts of 8-epi-PGF(2alpha) by rat glomeruli. In contrast, the total isoprostane fraction could be increased by menadione addition. These data provide further evidence for a radical-independent, but COX-dependent formation of 8-epi-PGF(2alpha) in renal tissue. Regarding the other isoprostanes, both radicals and COX enzymes contribute to their formation. Based on our data we assume that elevated release of vasoactive 8-epi-PGF(2alpha) has to be expected under conditions when the prostanoid system in the kidney is stimulated, e.g. under inflammatory conditions. Regarding renal oxidative injuries, the usefulness of 8-epi-PGF(2alpha) as a representative marker molecule of oxidative stress has to be questioned.

L103 ANSWER 5 OF 15 MEDLINE
ACCESSION NUMBER: 1998011870 MEDLINE
DOCUMENT NUMBER: 98011870 PubMed ID: 9351505
TITLE: Effects of ibuprofen enantiomers and its coenzyme A thioesters on human prostaglandin endoperoxide synthases.
AUTHOR: Neupert W; Brugger R; Euchenhofer C; Brune K; Geisslinger G
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology and Toxicology, University of Erlangen-Nurnberg, Erlangen, Germany.
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1997 Oct) 122 (3) 487-92. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199712

ENTRY DATE: Entered STN: 19980109
Last Updated on STN: 19980109
Entered Medline: 19971208

AB 1. Ibuprofen enantiomers and their respective coenzyme A thioesters were tested in human platelets and blood monocytes to determine their selectivity and potency as inhibitors of cyclo-oxygenase activity of prostaglandin endoperoxide synthase-1 (PGHS-1) and PGHS-2. 2. Human blood from volunteers was drawn and allowed to clot at 37 degrees C for 1 h in the presence of increasing concentrations of the test compounds (R-ibuprofen, S-ibuprofen, R-ibuprofenoyl-CoA, S-ibuprofenoyl-CoA, NS-398). Immunoreactive (ir) thromboxane B2 (TXB2) concentrations in serum were determined by a specific EIA assay as an index of the cyclo-oxygenase activity of platelet PGHS-1. 3. Heparin-treated blood from the same donors was incubated at 37 degrees C for 24 h with the same concentrations of the test compounds in the presence of lipopolysaccharide (LPS, 10 microg ml[-1]). The contribution of PGHS-1 was suppressed by pretreatment of the volunteers with aspirin (500 mg; 48 h before venepuncture). As a measure of LPS induced PGHS-2 activity immunoreactive prostaglandin E2 (irPGE2) plasma concentrations were determined by a specific EIA assay. 4. S-ibuprofen inhibited the activity of PGHS-1 (IC50 2.1 microM) and PGHS-2 (IC50 1.6 microM) equally. R-ibuprofen inhibited PGHS-1 (IC50 34.9) less potently than S-ibuprofen and showed no inhibition of PGHS-2 up to 250 microM. By contrast R-ibuprofenoyl-CoA thioester inhibited PGE2 production from LPS-stimulated monocytes almost two orders of magnitude more potently than the generation of TXB2 (IC50 5.6 vs 219 microM). 5. Western blotting of PGHS-2 after LPS induction of blood monocytes showed a concentration-dependent inhibition of PGHS-2 protein expression by ibuprofenoyl-CoA thioesters. 6. These data confirm that S-ibuprofen represents the active entity in the racemate with respect to cyclo-oxygenase activity. More importantly the data suggest a contribution of the R-enantiomer to therapeutic effects not only by chiral inversion to S-ibuprofen but also via inhibition of induction of PGHS-2 mediated by R-ibuprofenoyl-CoA thioester. 7. The data may explain why racemic ibuprofen is ranked as one of the safest non-steroidal anti-inflammatory drugs (NSAIDs) so far determined in epidemiological studies.

L103 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
ACCESSION NUMBER: 2002:123258 CAPLUS
DOCUMENT NUMBER: 136:163289
TITLE: Compositions and methods for detecting and quantifying **COX-2** activity and **2-arachidonylglycerol** metabolites and application to monitoring of inflammation and cancer
INVENTOR(S): Marnett, Lawrence J.; Kozak, Kevin R.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012549	A1	20020214	WO 2001-US24762	20010807

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001084747	A5	20020218	AU 2001-84747		20010807
US 2002064804	A1	20020530	US 2001-923637		20010807
US 2002106707	A1	20020808	US 2001-924082		20010807
PRIORITY APPLN. INFO.:			US 2000-223665P	P	20000807
			US 2001-302975P	P	20010703
			WO 2001-US24762	W	20010807

AB The present invention provides methods, compns. and kits for discriminating between COX-1 and COX-2 activity. In particular, the prevent invention provides for the detection and/or measurement of COX-2 activity in subjects, samples thereof, and in lab. tests. The present invention discloses that **2-arachidonylglycerol** is a COX-2 selective substrate which is metabolized by COX-2 to prostaglandin glycerol esters (PG-Gs) and that the diversity of PG-Gs parallels that or arachidonic acid derived metabolites of COX. The present invention also provides certain novel COX-2 selective metabolites including prostaglandin I2-glycerol ester (PGI2-G) and 6-keto-prostaglandin F1a.alpha.-glycerol ester. Methods and kits are described for detecting COX-2 activity comprising detecting PG-Gs including the novel PG-Gs disclosed herein. Uses for these methods and kits include the detection and monitoring of inflammation and tumors or cancer. Addnl. uses include the monitoring of test agents in assays to screen for COX-2 specific inhibitors and other lab. uses.

IT **53847-30-6D, 2-Arachidonylglycerol,** metabolites **329900-75-6, COX 2**
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); **ANST (Analytical study)**; BIOL (Biological study); USES (Uses)
(compns. and methods for detecting and quantifying **COX-2** activity and **2-arachidonylglycerol** metabolites and application to monitoring of inflammation and cancer)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	2001:105771 CAPLUS
DOCUMENT NUMBER:	134:141895
TITLE:	Gas chromatography-**mass spectrometry** analysis of endogenous cannabinoids in healthy and tumoral human brain and human cells in culture
AUTHOR(S):	Maccarrone, Mauro; Attina, Marina; Cartoni, Antonella; Bari, Monica; Finazzi-Agro, Alessandro
CORPORATE SOURCE:	Department of Experimental Medicine and Biochemical Sciences, University of Rome "Tor Vergata", Rome, I-00133, Italy
SOURCE:	Journal of Neurochemistry (2001), 76(2), 594-601 CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER:	Blackwell Science Ltd.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Endocannabinoids are lipid mediators thought to modulate central and peripheral neural functions. The authors report gas chromatog.-electron impact mass spectrometry anal. of human brain, showing that lipid exts. contain anandamide and 2-arachidonoylglycerol (2-AG), the most active endocannabinoids known to date. Human brain also contained the endocannabinoid-like compds. N-oleoylethanolamine, N-palmitoylethanolamine and N-stearoylethanolamine. Anandamide and 2-AG (0.16.+-.0.05 and 0.10.+-.0.05 nmol/mg protein, resp.) represented 7.7% and 4.8% of total endocannabinoid-like compds., resp. N-palmitoylethanolamine was the most abundant (50%), followed by N-oleoyl (23.6%) and N-stearoyl (13.9%) ethanolamines. A similar compn. in endocannabinoid-like compds. was found in human neuroblastoma CHP100 and lymphoma U937 cells, and also in rat brain. Remarkably, human meningioma specimens showed an approx. six-fold smaller content of all N-acylethanolamines, but not of 2-AG, and a similar

decrease was obsd. in a human glioblastoma. These ex vivo results fully support the purported roles of endocannabinoids in the nervous system.

IT **53847-30-6, 2-Arachidonylglycerol**
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study); PROC (Process)
(gas chromatog.-**mass spectrometry** anal. of endogenous cannabinoids in healthy and tumoral human brain and human cells in culture)

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:423397 CAPLUS
DOCUMENT NUMBER: 133:161886
TITLE: Polyunsaturated monoglycerides and a pregnadiene in defensive glands of the water beetle Agabus affinis
AUTHOR(S): Schaaf, Otmar; Dettner, Konrad
CORPORATE SOURCE: Department of Animal Ecology II, University of Bayreuth, Bayreuth, D-95440, Germany
SOURCE: Lipids (2000), 35(5), 543-550
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In addn. to the C21 steroid 15.alpha.-hydroxypregna-4,6-dien-3,20-dione, four 1- or 2-acylated polyunsatd. monoglycerides, 1- or 2-(cis-5,8,11,14-eicosatetraenoyl)glycerol and 1- or 2-(cis-5,8,11,14,17-eicosapentaenoyl)glycerol were identified as constituents of the prothoracic defensive gland secretion of the dytiscid beetle Agabus affinis by gas chromatog.-mass spectrometry of trimethylsilylated gland exts. In a feeding assay with minnows, synthetic samples of the two 2-acylated monoglycerides showed only a weak activity as a feeding deterrent. For that reason, other possible functions of the monoglycerides are discussed, such as roles as emulsifiers of cannabimimetics.

IT **53847-30-6**
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(polyunsatd. monoglycerides and pregnadiene in defensive glands of water beetle)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:8067 CAPLUS
DOCUMENT NUMBER: 132:262339
TITLE: A sensitive endocannabinoid assay. The simultaneous analysis of N-acylethanolamines and 2-monoacylglycerols
AUTHOR(S): Schmid, P. C.; Schwartz, K. D.; Smith, C. N.; Krebsbach, R. J.; Berdyshev, E. V.; Schmid, H. H. O.
CORPORATE SOURCE: Hormel Institute, University of Minnesota, Austin, MN, USA
SOURCE: Chemistry and Physics of Lipids (2000), 104(2), 185-191
CODEN: CPLIA4; ISSN: 0009-3084
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mammalian cells produce both N-arachidonoylethanolamine (20:4n-6 NAE, anandamide) and 2-arachidonoylglycerol (2-AG), lipid signaling mols. that

activate cannabinoid receptors. Because both agonists occur in the presence of receptor-inactive congeners, we have developed a sensitive method for the simultaneous assay of N-acylethanolamines (NAEs) and 2-monoacylglycerols (2-MAG). These lipid classes are isolated from total lipids by solid phase extn. and converted to tert-butyldimethylsilyl (tBDMS) derivs. in the presence of deuterated analogs. The tBDMS derivs. are analyzed by gas chromatog./mass spectrometry using selected ion monitoring programs specific for NAE and 2-MAG. Individual NAEs and 2-MAGs can be quantified in the nanogram and subnanogram range. The NAE and 2-MAG compns. of rat organs and cultured JB6 cells are reported.

IT **53847-30-6**
RL: ANT (Analyte); **ANST (Analytical study)**
(simultaneous anal. of N-acylethanolamines and 2-monoacylglycerols)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:797899 CAPLUS
DOCUMENT NUMBER: 132:90214
TITLE: Liquid chromatographic-**mass spectrometric** measurement of the endogenous cannabinoid **2-arachidonylglycerol** in the spinal cord and peripheral nervous system
AUTHOR(S): Huang, Susan M.; Strangman, Nicole M.; Walker, J. Michael
CORPORATE SOURCE: The Alan M Schrier Research Laboratory, Departments of Psychology and Neuroscience, Brown University, Providence, RI, 02912, USA
SOURCE: Zhongguo Yaoli Xuebao (1999), 20(12), 1098-1102
CODEN: CYLPDN; ISSN: 0253-9756
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AIM: To develop a sensitive method for measuring the putative endocannabinoid **2-arachidonylglycerol** (2-AG) in the peripheral and central nervous system. METHODS: A method using atm. pressure chem. ionization (APCI) liq. chromatog./mass spectrometry (LC/MS) was developed to det. the levels of 2-AG in methanol exts. of the rat lumbar spinal cord, dorsal root ganglion (DRG), and sciatic nerve. RESULTS: 2-AG was detected with high sensitivity and minimal sample prepn. The levels in the tissues analyzed were .ltoreq.pmol/mg wet wt. Similar levels were found in the spinal cord and the DRG, whereas approx. 7-fold lower levels were obsd. in the sciatic nerve. CONCLUSION: 2-AG is present in the peripheral nervous system, and the levels are markedly higher in cell bodies than those in axons.

IT **53847-30-6, 2-Arachidonylglycerol**
RL: ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); **ANST (Analytical study)**; BIOL (Biological study); OCCU (Occurrence)
(liq. chromatog.-**mass spectrometric** measurement of the endogenous cannabinoid **2-arachidonylglycerol** in the spinal cord and peripheral nervous system)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 11 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:139790 BIOSIS
DOCUMENT NUMBER: BA67:19790
TITLE: PRACTICAL ASPECTS OF LIQUID CHROMATOGRAPHY MASS SPECTROMETRY OF LIPIDS.
AUTHOR(S): PRIVETT O S; ERDAHL W L
CORPORATE SOURCE: HORMEL INST., UNIV. MINN., AUSTIN, MINN 55912, USA.
SOURCE: CHEM PHYS LIPIDS, (1978) 21 (4), 361-388.

CODEN: CPLIA4. ISSN: 0009-3084.
FILE SEGMENT: BA; OLD
LANGUAGE: English
AB Techniques for coupling liquid chromatography (LC) with mass spectrometry (MS) are reviewed and an interface is described for the analysis of lipids by MS. The interface for coupling LC with MS for lipid analysis is based on the moving wire transport principle using an endless stainless steel belt of novel construction. After evaporation of the solvent, the solute remains as a residue on the belt which transports it into a reactor where it is volatilized by evaporation or conversion to hydrocarbons. The volatile compounds are then fed into the source of a chemical ionization mass spectrometer for mass analysis by total or single ion monitoring as well as for structural identification or compositional analysis. The sensitivity of the system was approximately 1 ng/component separated in the eluate of a high efficiency column. The capabilities of the interface were demonstrated by its application to reference compounds representative of triglycerides, sterols, steryl esters, glyceryl ethers, glyceryl ether diesters, glycerophosphatides, sphingolipids, prostaglandins and fatty acid methyl esters. It also was applied to the analysis of methyl ester ozonides to demonstrate the use of LC-MS for the localization of double bonds in unsaturated fatty acids.

L103 ANSWER 12 OF 15 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1975:94628 BIOSIS
DOCUMENT NUMBER: BR11:94628
TITLE: INFLUENCE OF DI BUTYRYL CYCLIC AMP ON GLUCOSE AND FAT METABOLISM IN NORMAL AND DIABETIC RATS.
AUTHOR(S): ZANOBONI A; ZANOBONI-MUCIACCIA W
SOURCE: Experientia, (1975) 31 (4), 473-474.
CODEN: EXPEAM. ISSN: 0014-4754.
FILE SEGMENT: BR; OLD
LANGUAGE: Unavailable

L103 ANSWER 13 OF 15 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-227145 [28] WPIDS
CROSS REFERENCE: 2002-315364 [35]; 2002-556719 [59]
DOC. NO. NON-CPI: N2002-174333
DOC. NO. CPI: C2002-069177
TITLE: Detecting or measuring cyclooxygenase enzyme, COX-2 activity for monitoring inflammation and cancer, by detecting or measuring COX-2 enzymatic products especially prostaglandin ethanolamides in a sample.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): KOZAK, K R; MARNETT, L J
PATENT ASSIGNEE(S): (UYVA-N) UNIV VANDERBILT
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002012445	A1	20020214	(200228)*	EN	62

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001084753 A 20020218 (200244)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE

WO 2002012445 A1 WO 2001-US24796 20010807
AU 2001084753 A AU 2001-84753 20010807

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001084753 A	Based on	WO 200212445

PRIORITY APPLN. INFO: US 2001-302975P 20010703; US 2000-223665P 20000807

AB WO 200212445 A UPAB: 20020919
NOVELTY - Detecting or measuring an **activity** of a **cyclooxygenase-2** (**COX-2**) in a sample or a subject, comprising obtaining a sample of the subject and detecting or quantifying COX-2 specific enzymatic product, especially prostaglandin H2-ethanolamide (PGH2-EA) **metabolite** in the sample, is new.

DETAILED DESCRIPTION - Detecting or measuring an **activity** of a **cyclooxygenase-2** (**COX-2**) in a sample or a subject, comprising obtaining a sample of the subject and detecting or quantifying COX-2 specific enzymatic product, especially prostaglandin H2-ethanolamide (PGH2-EA) **metabolite** in the sample, is new. Arachidonyl ethanolamide (AEA) is administered to the subject, prior to sampling.

INDEPENDENT CLAIMS are also included for the following:

(1) selectively detecting **COX-2 activity** in a sample, comprising:

(a) adding a COX-2 selective substrate to the sample; and

(b) detecting a **metabolite** of the COX-2 selective substrate, which indicates the **COX-2 activity**;

(2) measuring COX-1 activity in a sample, comprising:

(a) adding a non-selective COX substrate and a COX-2 selective substrate to the sample;

(b) measuring a first amount of a **metabolite** of the COX-1 substrate in the sample after a period of time, and a second amount of a **metabolite** of the COX-2 selective substrate **metabolite**; and

(c) comparing the first and second amounts;

(3) distinguishing **COX-2 activity** from COX-1 **activity** in a subject, comprising:

(a) administering a COX-1 substrate and COX-2 selective substrate to the subject;

(b) obtaining a sample from the subject after a period of time;

(c) determining a first amount of a **metabolite** of the COX-1 substrate and a second amount of **metabolite** of the COX-2 selective substrate; and

(d) comparing the first amount to the second amount;

(4) a composition (C) comprising a label for detecting PGH2-EA **metabolite**;

(5) making an isolated PGH2-EA **metabolite** including a label, by reacting a COX-2 **metabolite** with a labeled EA, or reacting a labeled COX-2 **metabolite** with a EA;

(6) an article of manufacture (kit), comprising packaged together a vessel containing labeled PGH2-EA **metabolite** or an isolated antibody against PGH2-EA **metabolite**, and a set of instructions delineating a process of measuring a **COX-2** specific **activity**;

(7) an antibody that binds specifically to a COX-2 **metabolite** EA, PGH2-EA **metabolite** or PGE2-EA;

(8) making an antibody that binds specifically PGH2-EA **metabolites** from a PG with substituted cyclopentyl and amide moieties, by protecting the cyclopentyl substituents and ethanolamide

moiety of the PG to produce a protected PG-EA, chemically modifying the protected PG-EA with an appropriate conjugate to produce a protected, conjugated PG-EA, deprotecting the conjugated PG-EA to generate an immunogen and purifying the immunogen;

(9) a composition comprising PGD2-EA or their salts; and

(10) a composition comprising a 6-keto-PGF(1 alpha)-ethanolamide or their salts.

ACTIVITY - Antipsoriatic; Cardiant; Cytostatic; Anti-HIV (human immunodeficiency virus); Antibacterial; Immunosuppressive; Antiinflammatory; Vasotropic.

No biological data is given.

MECHANISM OF ACTION - None given.

USE - The method is useful for detecting or measuring **COX-2 activity** in a sample such as urine, blood, plasma, cerebrospinal fluid, saliva, sputum, bile, joint fluid, biopsy, and conditioned media from a cell culture. Detecting the **activity** of **COX-2** enzyme is useful for screening for a tumor in a subject, detecting and measuring an inflammation in a subject, and measuring **activity** of **COX-2** is useful for screening for a tumor in a subject, monitoring an anti-cancer and anti-inflammation therapy in a subject. (All claimed). The method is also useful in detecting or treating non-malignant or immunologically-related cell-proliferative diseases such as psoriasis, pemphigus vulgaris, Behcet's syndrome, acute respiratory distress syndrome (ARDS), ischemic heart disease, post-dialysis syndrome, leukemia, acquired immune deficiency syndrome, septic shock, and other types of acute inflammation, and lipid histiocytosis, and facilitates the detection, measurement and treatment of any disorder which is etiologically linked to the inflammatory process. The compositions and kits are useful for screening candidate molecules for their ability to regulate COX-2 using cultured cells, tissues or whole animals.

ADVANTAGE - The use of PGH2-EA **metabolite** quantification allows for a relatively non-invasive quantification of **COX-2 activity** in vivo. The noninvasive nature allows for much broader testing increasing the sample size in these studies and permitting rapid and statistically significant association between **COX-2 activity** and the pathology under study. Quantification of PGH2-EA **metabolites** in vivo provides a simple assay for assessing the in vivo efficacy of newly developed COX-2 inhibitors.

Dwg.0/13

L103 ANSWER 14 OF 15 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-556719 [59] WPIDS
CROSS REFERENCE: 2002-227145 [28]; 2002-315364 [35]
DOC. NO. NON-CPI: N2002-440644
DOC. NO. CPI: C2002-157800
TITLE: Detecting or measuring **activity** of **cyclooxygenase-2** enzyme for detecting tumor or inflammation, by measuring **cyclooxygenase-2** specific **metabolite** of 2-**arachidonylglycerol** in sample.
DERWENT CLASS: B04 D16 P31 S03
INVENTOR(S): KOZAK, K R; MARNETT, L J
PATENT ASSIGNEE(S): (KOZA-I) KOZAK K R; (MARN-I) MARNETT L J
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2002064804	A1	20020530	(200259)*		29

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002064804 A1	Provisional	US 2000-223665P	20000807
	Provisional	US 2001-302975P	20010703
		US 2001-923637	20010807

PRIORITY APPLN. INFO: US 2001-923637 20010807; US 2000-223665P 20000807; US 2001-302975P 20010703

AB US2002064804 A UPAB: 20020916

NOVELTY - Detecting (M1) or measuring an **activity** of cyclooxygenase (**COX**)-**2** enzyme (I) in a subject, involves obtaining sample of the subject and detecting or measuring **COX-2** specific **metabolite** of 2-**arachidonylglycerol** or **COX-2** selective substrate in the sample, where the presence of the **COX-2** specific **metabolite** in the sample indicates the **activity** of the **COX-2** enzyme in the subject.

DETAILED DESCRIPTION - Detecting (M1) or measuring an **activity** of cyclooxygenase (**COX**)-**2** enzyme (I) in a subject, involves obtaining sample of the subject and detecting a **COX-2** specific **metabolite** of 2-**arachidonylglycerol**, or **COX-2** selective substrate in the sample, where the presence of the **COX-2** specific **metabolite** in the sample indicates the **activity** of the **COX-2** enzyme in the subject. Alternatively, M1 involves adding a **COX-2** selective substrate to the sample or administering an effective amount of a **COX-2** selective substrate to the subject and detecting a **metabolite** of **COX-2** selective substrate in the sample or in the subject, respectively, where the presence of **metabolite** indicates the **COX-2 activity**.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition (I) comprising a **COX-2** selective **metabolite** including a label for detecting the **metabolite**, **prostaglandin** D2-**glycerol ester** or 6-keto-**prostaglandin** F(1 alpha)-**glycerol ester**;

(2) making (M2) a labeled **COX-2** selective **metabolite**, involves reacting a **COX-2 metabolite** with a labeled glycerol, reacting a labeled **COX-2 metabolite** with glycerol, or reacting a labeled 2-**arachidonylglycerol** with a **COX-2** enzyme to form the labeled **COX-2** selective **metabolite**;

(3) a device (II) comprising a vessel containing an isolated antibody against a **COX-2** selective **metabolite**; or at least one labeled **COX-2** selective **metabolite**, and a set of instructions delineating a process of detecting an **activity** of a **COX-2** enzyme;

(4) an antibody (III) that binds specifically to **prostaglandin glyceryl ester** or 6-keto-**prostaglandin** F(1 alpha)-**glycerol ester**; and

(5) preparing (M3) antigen for the manufacture of an antibody that binds specifically to a glyceryl-prostaglandin having one or more substituted cyclopentyl and ester groups, involves protecting the substituted cyclopentyl and **ester** groups of the **glyceryl-prostaglandin**, haptenizing the protected glyceryl-prostaglandin, deprotecting one or more substituted cylopentyl and ester groups of the haptenized glyceryl-prostaglandin, and purifying the haptenized glyceryl-prostaglandin.

ACTIVITY - Antipsoriatic; Antiinflammatory; Vasotropic; Anti-HIV;

Cytostatic; Respiratory-Gen; Cardiant; Antibacterial; Immunosuppressive.
No supporting data is given.

MECHANISM OF ACTION - None given.

USE - M1 is useful for detecting or measuring an **activity** of **COX-2** enzyme. M1 is also useful for screening or detecting a tumor or inflammation in a subject (human), involves obtaining a sample of the subject, and detecting a **COX-2** specific **metabolite** in the sample, where the presence of the **COX-2** specific **metabolite** is indicative of the tumor or inflammation in the subject, and relating the amount of the **COX-2** specific **metabolite** to stages of tumor. M1 is further useful for monitoring an anticancer or antiinflammatory treatment in a patient, which involves obtaining a first sample of a patient, measuring first amount of **COX-2** specific **metabolite** in the first sample, obtaining a second sample of the patient after the anticancer or antiinflammatory treatment, measuring a second amount of the **COX-2** specific **metabolite** in the second sample, and determining a change in the second amount relative to the first amount, where the change indicates the effectiveness of the treatment (all claimed). M1 is useful for detecting a disease such as inflammation, cancer, neurodegeneration, and/or hyperalgesia, for evaluating the effectiveness of therapy and for developing new treatments for the diseases, and for monitoring test agents in assays to screen for **COX-2** specific inhibitors. (I) is useful for treating non-malignant or immunological-related cell-proliferative diseases such as psoriasis, pemphigus vulgaris, Behcet's syndrome, acute respiratory distress syndrome (ARDS), ischemic heart disease, post-dialysis syndrome, leukemia, acquired immune deficiency syndrome, septic shock and other types of acute and chronic inflammation, and lipid histiocytosis.

ADVANTAGE - The noninvasive nature of M1 allows for much broader testing, increasing the sample size in these studies and permitting rapid and statistically significant association between **COX-2** and the pathology under study. Using M1 it is possible for testing patients before disease signs are evident that allows assessing the role of **COX-2** in disease development and progression in contrast to post-mortem studies which evaluate the role of **COX-2** long after the disease process begins. Quantification of PG-Gs in vivo provides a simple assay for assessing the in vivo efficacy of newly developed **COX-2** inhibitors.

Dwg.0/21

L103 ANSWER 15 OF 15 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-024086 [02] WPIDS
DOC. NO. CPI: C1999-007344
TITLE: Treating pain and inflammation in dogs - using carprofen compounds as cyclo-oxygenase-2 selective inhibitors.
DERWENT CLASS: B03 B05 C02 C03
INVENTOR(S): LUNDY, K M; RICKETTS, A P; LUNDBY, K M
PATENT ASSIGNEE(S): (PFIZ) PFIZER INC
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9850033	A1	19981112	(199902)*	EN	83
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9869321	A	19981127	(199915)		
ZA 9803722	A	19991229	(200006)		83

NO 9905389 A 20000104 (200013)
EP 988034 A1 20000329 (200020) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI
BR 9808720 A 20000711 (200041)
CN 1255059 A 20000531 (200045)
JP 2000513020 W 20001003 (200052) 101
HU 2000001286 A2 20001128 (200103)
MX 9910148 A1 20000201 (200123)
CZ 9903896 A3 20010516 (200132)
KR 2001012300 A 20010215 (200154)
SK 9901481 A3 20010911 (200159)
NZ 500183 A 20020426 (200236)
AU 2002038232 A 20020620 (200252)#

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9850033	A1		WO 1998-IB662	19980501
AU 9869321	A		AU 1998-69321	19980501
ZA 9803722	A		ZA 1998-3722	19980504
NO 9905389	A		WO 1998-IB662	19980501
			NO 1999-5389	19991104
EP 988034	A1		EP 1998-915041	19980501
			WO 1998-IB662	19980501
BR 9808720	A		BR 1998-8720	19980501
			WO 1998-IB662	19980501
CN 1255059	A		CN 1998-804845	19980501
JP 2000513020	W		JP 1998-547869	19980501
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HU 2000001286	A2		WO 1998-IB662	19980501
			HU 2000-1286	19980501
MX 9910148	A1		MX 1999-10148	19991104
CZ 9903896	A3		WO 1998-IB662	19980501
			CZ 1999-3896	19980501
KR 2001012300	A		KR 1999-710252	19991105
SK 9901481	A3		WO 1998-IB662	19980501
			SK 1999-1481	19980501
NZ 500183	A		NZ 1998-500183	19980430
			WO 1998-IB662	19980501
AU 2002038232	A	Div ex	AU 1998-69321	19980501
			AU 2002-38232	20020508

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9869321	A	Based on	WO 9850033
EP 988034	A1	Based on	WO 9850033
BR 9808720	A	Based on	WO 9850033
JP 2000513020	W	Based on	WO 9850033
HU 2000001286	A2	Based on	WO 9850033
CZ 9903896	A3	Based on	WO 9850033
SK 9901481	A3	Based on	WO 9850033
NZ 500183	A	Div in	NZ 516914
		Based on	WO 9850033

PRIORITY APPLN. INFO: US 1997-45635P 19970505; AU 2002-38232 20020508

AB WO 9850033 A UPAB: 19990302
Treating pain and inflammation processes and diseases associated with the **activity** of inducible **cyclo-oxygenase-**

2 (**COX-2**) in dogs (Canis familiaris) while reducing or eliminating undesirable side-effects associated with simultaneous inhibition of the activity of COX-1 by selectively inhibiting COX2 activity with reference to COX-1 **activity**, where the selectivity ratio of **COX-2**:COX-1 **activity** inhibition is at least 3:1 based on ex vivo inhibition levels in whole blood measured at a dose giving at least 80% COX2 inhibition, comprises administering a carprofen derivative of formula (I) or its salt, prodrugs or **metabolites** as a selective COX-2 inhibitor. R2 = (C(X)(Y)n-CO-A; A = OH, 1-4C alkoxy, NH2, hydroxyamino, mono(1-2C)alkylamino or di(1-2C)alkylamino; X, Y = H or 1-2C alkyl; n = 1 or 2; R6 = halo, 1-3C alkyl, CF3 or NO2; R9 = H, 1-2C alkyl or phenyl or phenyl(1-2C)alkyl (optionally phenyl monosubstituted by F or Cl), COR or COOR1; R = 1-2C alkyl or phenyl optionally mono-substituted by F or Cl and R1 = 1-2C alkyl. Also claimed is a method of treating or preventing inflammatory processes in dogs in which (I) is used in combination with at least 1 other active agent under the following conditions: (A) where a joint is seriously inflamed and infected at the same time by bacteria, fungi, protozoa and/or virus, (I) is administered in combination with antibiotic, antifungal, antiprotozoal and/or antiviral agents; (B) where a multi-fold treatment of pain and inflammation is required (I) is administered in combination with inhibitors of other mediators of inflammation comprising at least 1 of (a) non steroidal antiinflammatory drugs; (b) H1-receptor antagonists; (c) kinin-B1 and B2 receptor antagonists; (d) prostaglandin inhibitors comprising PGD, PGF, PGI2 or PGE receptor antagonists; (e) thrombane A2 inhibitors; (f) 5- and 12-lipoxygenase inhibitors; (g) leukotriene LTC4, LTD4/LTE4 and LTB4 inhibitors; (h) platelet activating factor receptor antagonists; (i) gold in the form of an aurothio group together with at least 1 hydrophilic groups; (j) immunosuppressive agents comprising cyclosporine, azathioprine or methotrexate; (k) antiinflammatory glucocorticoids; (l) penicillamine; (m) hydroxychloroquine; (n) antigout agents including colchicine, xanthine oxidase inhibitors including allopurinol and uricosuric agents selected from probenecid, sulfinpyrazone and benzbromarone; (C) where older dogs are treated for disease conditions and symptoms in geriatric dogs, (I) is administered with (1) at least 1 of cognitive therapeutics to counteract memory loss and impairment, (2) anti-hypertensives and other cardiovascular drugs to offset the consequences of atherosclerosis, hypertension, myocardial ischaemia, angina, congestive heart failure and myocardial infarction selected from: (a) diuretics; (b) vasodilators; (c) beta -adrenergic receptor antagonists; (d) angiotensin-II converting enzyme inhibitors optionally together with neutral endopeptidase inhibitors; (e) angiotensin-II receptor antagonists; (f) renin inhibitors; (g) calcium channel blockers; (h) sympatholytic agents; (i) alpha -adrenergic agonists; (j) alpha -adrenergic receptor antagonists and (k) HMG-CoA-reductase inhibitors; (3) antineoplastic agents selected from antimitotic agents selected from vinca alkaloids e.g. vinblastine and vincristine; (4) growth hormone secretagogues; (5) strong analgesics; (6) local and systemic anaesthetics and (7) H2-receptor antagonists, proton pump inhibitors and other gastroprotective agents.

USE - The methods are used to treat and/or prevent pain and inflammatory processes and diseases associated with the **activity** of inducible **COX-2** in members of the species Canis familiaris. The dosage is 0.01-20 (especially 0.5-8) mg/kg/day.

ADVANTAGE - (I) reduce the side effects experienced with many non-steroidal anti-inflammatory agents including disturbance and irritation of the gastrointestinal mucosa leading to ulceration, haemorrhage and eventually perforation and peritonitis.

Dwg.0/0

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FILE 'REGISTRY' ENTERED AT 14:01:40 ON 21 NOV 2002
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STRUCTURE FILE UPDATES:   20 NOV 2002  HIGHEST RN 474043-36-2
DICTIONARY FILE UPDATES:  20 NOV 2002  HIGHEST RN 474043-36-2

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

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Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

L8                STR
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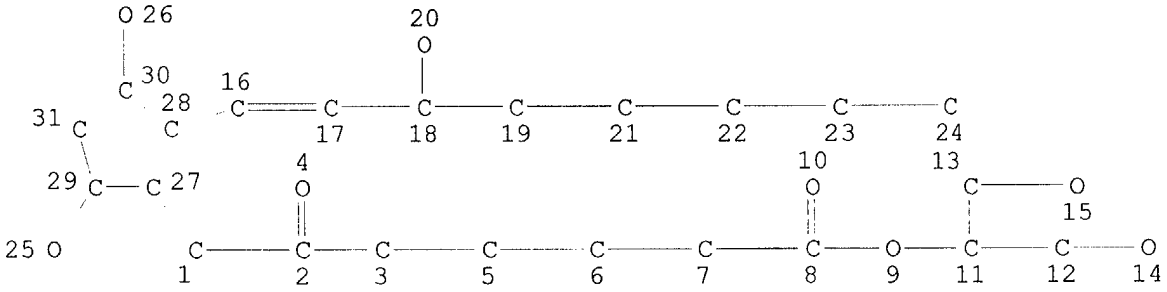

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  31

STEREO ATTRIBUTES: NONE
L10             1 SEA FILE=REGISTRY FAM FUL L8

100.0% PROCESSED     30 ITERATIONS                    1 ANSWERS
SEARCH TIME: 00.00.02
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family search done on structure of species to pick up stereoisomers, isotopically labelled forms, multi-component substances, and salts

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=> fil capl; d que nos l11; fil toxcenter; d que nos l13
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FILE COVERS 1907 - 21 Nov 2002 VOL 137 ISS 21
FILE LAST UPDATED: 20 Nov 2002 (20021120/ED)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L8 STR
L10 1 SEA FILE=REGISTRY FAM FUL L8
L11 1 SEA FILE=CAPLUS ABB=ON L10

FILE 'TOXCENTER' ENTERED AT 14:01:53 ON 21 NOV 2002
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FILE COVERS 1907 TO 19 Nov 2002 (20021119/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

The MEDLINE file segment has been reloaded. See HELP RLOAD for details.

Thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

L8 STR
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L13 1 SEA FILE=TOXCENTER ABB=ON L10

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FILE 'TOXCENTER' ENTERED AT 14:01:58 ON 21 NOV 2002
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PROCESSING COMPLETED FOR L11
PROCESSING COMPLETED FOR L13
L104 1 DUP REM L11 L13 (1 DUPLICATE REMOVED)
ANSWER '1' FROM FILE CAPLUS

=> d ibib abs hitstr; fil hom

L104 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2002:123258 CAPLUS
DOCUMENT NUMBER: 136:163289
TITLE: Compositions and methods for detecting and quantifying COX-2 activity and 2-arachidonylglycerol metabolites and application to monitoring of inflammation and cancer
INVENTOR(S): Marnett, Lawrence J.; Kozak, Kevin R.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012549	A1	20020214	WO 2001-US24762	20010807
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001084747	A5	20020218	AU 2001-84747	20010807
US 2002064804	A1	20020530	US 2001-923637	20010807
US 2002106707	A1	20020808	US 2001-924082	20010807

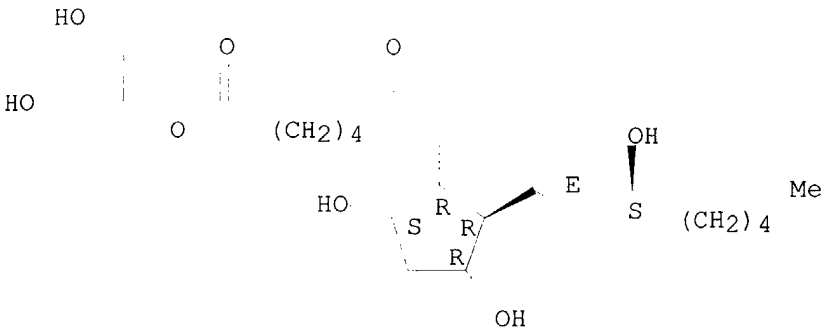
PRIORITY APPLN. INFO.:
US 2000-223665P P 20000807
US 2001-302975P P 20010703
WO 2001-US24762 W 20010807

AB The present invention provides methods, compns. and kits for discriminating between COX-1 and COX-2 activity. In particular, the prevent invention provides for the detection and/or measurement of COX-2 activity in subjects, samples thereof, and in lab. tests. The present invention discloses that 2-arachidonylglycerol is a COX-2 selective substrate which is metabolized by COX-2 to prostaglandin glycerol esters (PG-Gs) and that the diversity of PG-Gs parallels that or arachidonic acid derived metabolites of COX. The present invention also provides certain novel COX-2 selective metabolites including prostaglandin I2-glycerol ester (PGI2-G) and 6-keto-prostaglandin F1a.alpha.-glycerol ester. Methods and kits are described for detecting COX-2 activity comprising detecting PG-Gs including the novel PG-Gs disclosed herein. Uses for these methods and kits include the detection and monitoring of inflammation and tumors or cancer. Addnl. uses include the monitoring of test agents in assays to screen for COX-2 specific inhibitors and other lab. uses.

IT **398147-52-9**
RL: ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(compns. and methods for detecting and quantifying COX-2 activity and 2-arachidonylglycerol metabolites and application to monitoring of inflammation and cancer)

RN 398147-52-9 CAPLUS
CN Prost-13-en-1-oic acid, 9,11,15-trihydroxy-6-oxo-, 2-hydroxy-1-(hydroxymethyl)ethyl ester, (9.alpha.,11.alpha.,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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